erenced, for example "edema" and "renal failure," because the references classified under the primary heading "anuria" will be omitted. Even the more sophisticated searches[4] provide incomplete listings more often than one would expect. Unfamiliarity of the searcher with the capabilities of the system or unusual needs of the searcher account without doubt for at least a part of the missing references. But incomplete and nonuniform coding of the articles accounts for a large share of these omissions, I suspect.

A drastic improvement of the bibliographic search will follow a uniform coding. The currently developed Unified Medical Language System[4] will contribute to the improvement of article retrieval. I suggest that active involvement of the editorial staff of medical journals in the process of article classification and coding would be equally important. Currently, many journals do not publish "key" or "index" words. Even journals publishing "index" words provided by the authors do not provide much help because often these index words are not parts of the existing coding system and are not utilized by the coding services. I propose that journals should publish index words and that they should specify in their instructions to authors that only index words conforming to one of the existing classifications, preferably MeSH, will be published. Editorial and reviewing procedures should address this important part of the manuscripts. This process should eliminate, in most instances, the need for changes by the coding services and should give the authors an opportunity to specify their preference for classification of their work.

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Dietary Cholesterol and Atherosclerosis

TO THE EDITOR: After 40 years and probably at least as many millions of dollars spent in the attempt, a direct cause-effect relationship between dietary cholesterol and atherosclerosis has not yet been proved; nevertheless, it has come to be accepted as common knowledge. In her otherwise exemplary, informative and well documented (46 references) article "Diet and Cancer—Should We Change What We Eat?" in the January issue,[1] Susan Desmond, MD, says the following: "coronary artery disease mortality (linked to a high-cholesterol diet). . . ." This is undocumented in the article, and a literature review is not likely to yield significant support.

The basis for this linkage is, as everyone knows, the well-documented decrease in deaths from myocardial infarction in Europe during World War II, when diets were necessarily low in cholesterol. That this concurrence was *not* in fact a cause-effect relationship has been clearly shown by review of autopsy records in Graz, Austria.[2] While deaths from myocardial infarction were reduced by 75% during the war, incidence of atherosclerotic coronary artery disease found at autopsy actually increased. There was a pronounced increase in mortality from infection from 1939 to 1944, with "extra deaths from tuberculosis alone threefold greater than the drop in heart attacks."

Dr Barnes makes a good case for the association of both infectious disease and coronary artery disease with thyroid deficiency,[2] which he calls "the missing link in the genesis of atherosclerosis." By assiduous control of hypothyroidism, relying on basal temperature, in 1,569 cases followed over 8,824 patient-years, he found just four new cases of coronary artery disease.

Dr Barnes' work cannot be said to be controversial since it has been completely ignored, while the myth of high-cholesterol diet/coronary artery disease linkage persists. The findings of a single obscure physician need not be taken at face value, but the reported greater than 90% decrease in incidence of coronary artery disease should be sufficiently provocative to elicit further study.

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Dr Desmond Responds

TO THE EDITOR: In my article on diet and cancer,[1] I attempted a thorough review of the topic based upon an extensive literature search through many more than the 46 references cited in the article. It is because of this thorough research that I felt qualified to come to conclusions regarding what general dietary guidelines may help to decrease the risk of cancer. Be assured that there has been no direct cause and effect shown between any of these dietary components and cancer. Indeed, it is rare in medicine that one can be dogmatic about proving causality. Nevertheless, as physicians and scientists, we must make causal judgments. To quote A. B. Hill, "All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have or to postpone the action that it appears to demand at a certain time."[2]

One area of science in which a great deal of advancing knowledge has accumulated recently is that of lipids and atherosclerosis. Dr Wolfstein has questioned whether coronary artery disease can be said to be linked to a high cholesterol diet. As my personal expertise does not extend to this area, I would like to rely on the National Institutes of Health Consensus Conference to reply to this criticism.[3] In December 1984 this group of lipoprotein experts, cardiologists, primary care physicians, epidemiologists, and others met to hear a series of expert presentations and to review all of the available data on lowering blood cholesterol to prevent heart disease. They concluded that "Elevated blood cholesterol is a major cause of coronary artery disease. It has been established beyond a reasonable doubt that lowering definitely elevated blood cholesterol levels will reduce the risk of heart attacks due to coronary heart disease." They also noted, "There is no doubt that appropriate changes in our diet will reduce blood cholesterol levels." These dietary changes include lowering intake of dietary total fat, saturated fat and cholesterol. Clearly, the conclusions of this Consensus Conference would

support the statement that coronary artery disease mortality has been linked to a high-cholesterol diet.

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The Role of Irradiation

TO THE EDITOR: I would like to comment on the article "Subacute Leukoencephalopathy Complicating Acute Lymphoblastic Leukemia" in the February 1987 issue.[1] Cranial irradiation was implicated as a probable cause of the patient's severe delayed leukoencephalopathy. However, in the case presentation, no mention of irradiation was made. We are not told when in the course of the illness the patient received radiation treatment, what area was treated or the total dose and daily fractionation. These factors are all very important in evaluating the contribution of irradiation to the patient's clinical course. Although I do not question the probable role of the irradiation in the patient's illness, I do feel that we in the medical community have a responsibility to discuss radiation effects in objective and specific terms, with reference to the large body of available information.

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Drs Filloux and Townsend Respond

TO THE EDITOR: Dr Cole is quite justified in inquiring about the details of craniospinal irradiation in this patient, as a single sentence providing this information was inadvertently omitted from the final draft of our manuscript. The patient received 2,360 rads of cranial irradiation in 12 fractions over a three-week period beginning three months after the discovery of malignant cells in the cerebrospinal fluid, and 1,800 rads to the spinal axis in ten fractions during the same period. We regret this serious omission and thank Dr Cole for bringing it to our attention.

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Incidence of Cough Associated With Captopril Therapy

TO THE EDITOR: In an article in the February issue, McNally[1] discusses the incidence and potential pathophysiology of cough occurring in association with captopril therapy. The current labeling for captopril lists cough (along with several other adverse reactions) as occurring "in about 0.5 to 2 percent of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials" involving captopril.

The published data cited for the 5% to 15% incidence used by the author are biased by the fact that the frequencies reported describe limited patient groups for whom cough has been a problem—in fact, the author's personal experience would suggest an even higher incidence.

From a data base of approximately 12,000 patients who received captopril in controlled clinical trials, 105 (0.9%) had cough reported as an adverse reaction. The vagaries of the postmarketing experience preclude a reliable frequency determination of any adverse reaction, since both the reaction (numerator) and the population exposed to the drug (denominator) cannot be easily quantified with any degree of accuracy.

Cough occurring in association with angiotensin-converting enzyme inhibitors is a recognized clinical entity,[2,3] albeit poorly understood. The incidence appears to be less than 2% when large groups of patients are reviewed, and individual clinical experiences must be analyzed in this context.

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